REMARKS

Claims 1-50 are all the claims pending in the application; claims 20-30 and 45-50 have been withdrawn from consideration; claims 1-19 and 31-44 have been rejected.

Claims 1-30, 39 and 47-48 are being canceled, and claims 51-72 are being added. Upon entry of this amendment, claims 31-38, 40-46, and 49-72 will be pending.

Support for the amendment to claim 40 may be found in paragraph 14 of the specification.

Support for new claims 51, 52 and 65 may be found in paragraph 16 of the specification.

New claims 69 and 70 are fully supported by original (now canceled) claim 39. Support for recitation of an antibody "that binds the same epitope" in place of "functional equivalents" may be found, for example, in paragraph 66 of the specification where it is noted that functional equivalents have binding characteristics comparable to other antibodies.

Support for the remainder of the new claims can be found in the canceled claims as follows:

New claim	Canceled claim	New claim	Canceled claim
53	2, 9-11	62	21
54	2, 12-14	63	24
55	4	64	25
56	15 (and in ¶14)	66	26-27
57	16	67	26-27
58	17	68	28
59	18	71	3
60	19	72	3
61	20		

No new matter has been added. Entry of this amendment is respectfully requested.

I. Restriction/Election of Species Requirement

In paragraphs 1-4 of the Office Action, the Examiner acknowledges Applicants' election of claims 1-19 and 31-44 for prosecution on the merits. The Examiner also indicates that the

election of species requirement has been withdrawn for all species. As such, the examination of the elected claims included both anti-Muc1 and anti-Muc16 antibodies, as well as each of the cytotoxic agents recited in the claims.

Applicants reiterate their request for rejoinder of method claims 20-30 and 45-50 (claims 45, 46, 49-52 and 61-68 upon entry of the instant amendment) upon allowance of the product claims from which they depend.

II. Rejection Under 35 U.S.C. §112

A. At paragraph 6 of the Office Action, claim 39 is rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

The Examiner has objected to the term "functional equivalent" as being unclear, for example, whether the term applies to the binding affinity of the antibody, or its avidity, or its specificity.

Included herewith is an amendment to the claims such that claim 39 is being replaced by new claims 69 and 70, thus making this rejection moot. New claims 69 and 70 recite an antibody "that binds the same epitope as" in place of a "functional equivalent." Applicants respectfully assert that new claims 69 and 70 are definite as written.

B. At paragraph 8 of the Office Action, claims 31-44 are rejected under 35 U.S.C. §112, first paragraph, as being non-enabled.

The Examiner states that because information pertaining to the deposit of the claimed hybridomas has not been provided, the claims to the hybridomas are not enabled.

Applicants respectfully note that the deposit information for each of the four deposited hybridomas is provided in paragraph [140] of the specification, including the name and address of the depository agency. Because the accession numbers had not been provided by the ATCC at the time the application was filed, blanks were left in paragraph [140] and in the claims. A preliminary amendment was filed October 6, 2005, filing in the blanks with the corresponding accession numbers in paragraph [140] and in the claims. Copies of the deposit receipts from the ATCC were included with the preliminary amendment, and it was stated in the preliminary amendment that all restrictions on the availability of the deposited material will be removed upon granting of the patent.

To further ensure that all of the requirements are met regarding biological deposits, enclosed herewith is a Declaration by Applicants that the deposit were accepted by an approved depository agency under the terms of the Budapest Treaty, and that all restrictions on the availability of the deposited materials will be removed upon granting of the patent

As each of the requirements with regard to biological deposits has thus been met, Applicants respectfully request reconsideration and withdrawal of this rejection.

III. Rejection Under 35 U.S.C. §102

A. At paragraph 10 of the Office Action, claim 1 is rejected under 35 U.S.C. §102(b) as being anticipated by Radosevich et al. (USP 6,166,176, issued Dec. 26, 2000).

The Examiner states that because Radosevich teaches monoclonal antibodies to an antigen that is not found in serum, Radosevich anticipates claims to an antibody that specifically binds to an epitope of a non-shed extracellular portion of an antigen as recited in claim 1.

Included herewith is an amendment to the claims such that claim 1 has been replaced by new claim 53 which recites antibodies that bind to specific portions of Muc1 (the amino acid sequences of SEQ ID NOs:8, 9, 10 and 12). Radosevich does not teach antibodies that bind to any portion of Muc1, let alone the portions of Muc1 set forth in SEQ ID NOs:8, 9, 10 and 12.

As Radosevich does not teach each and every element of claim 1 (replaced by claim 53), Applicants respectfully request reconsideration and withdrawal of this rejection.

B. At paragraph 11 of the Office Action, claims 1-3 and 9-11 are rejected under 35 U.S.C. §102(b) as being anticipated by Hartman et al. (Int. J. Cancer, 1999) as evidenced by Zrihan-Licht et al. (Eur. J. Biochem., 1994) and Parry et al. (Biochem. Biophys. Res. Comm., 2001).

Briefly, the Examiner states that Hartman teaches five antibodies that would be expected to bind to the non-shed extracellular portion of Muc1, as evidenced by Zrihan-Licht and Parry.

Included herewith is an amendment to the claims such that claim 1 has been replaced by new claim 53 which recites antibodies that bind to specific portions of Muc1 (the amino acid sequences of SEQ ID NOs:8, 9, 10 and 12).

Hartman does not teach antibodies that bind to any of the portions of Muc1 recited in new claim 53 (SEQ ID NOs:8, 9, 10 and 12). As shown in Appendix A, Hartman teaches a 255 amino acid portion of Muc1 (MucI/Y). Hartman also teaches six antibodies that bind to specific portions of Muc1 (6E6/2, 7D10/4, 9G2/6, 6C4/5, 6D3/12 and 10D/2). Hartman used deletion analysis to show that the antibodies bind to different regions of the mature version of MUC1/Y (lacking the signal peptide; beginning at the "1" above the top line of amino acid sequence shown in Appendix A). Specifically, Hartman found that antibody 6E6/2 binds to a region of MUC1/Y between amino acids 30 and 67 of the mature version of MUC1/Y (see the numbering and dashed lines above the amino acid sequence in Appendix A). Antibodies 7D10/4, 9G2/6 and 6C4/5 bind to a region of MUC1/Y between amino acids 68 and 87 of the mature version of MUC1/Y. Antibody 6D3/12 was found to bind to a region of MUC1/Y between amino acids 88 and 108 of the mature version of MUC1/Y. Antibody 10D2/36 was found to bind to a region of MUC1/Y between amino acids 118 and 131 of the mature version of MUC1/Y.

The four portions of Muc1 recited in new claim 53 as anti-Muc1 antibody epitopes (SEQ ID NOs:8, 9, 10 and 12) are also shown in Appendix A. These four sequences are shown below the amino acid sequence. The numbering corresponding to these four peptides corresponds to the non-shed extracellular domain of Muc1 set forth in SEQ ID NO:1 of the instant application.

A comparison of the epitopes recognized by the antibodies of Hartman, with those recognized by the antibodies of new claim 53, reveals that none of the Hartman epitopes correspond to the epitopes as recited in new claim 53. As such, the skilled artisan would not expect the antibodies of Hartman to bind the epitopes recited in claim. Accordingly, Hartman does not teach each and every element of new claim 53.

Hartman also does not teach a hybridoma that produces an antibody of claim 1 (new claim 53), as recited in claim 3 (new claim 71).

Furthermore, Hartman does not teach antibodies that bind to Muc16. Claim 2 has been replaced by new claim 54 which recites antibodies that bind to specific portions of Muc16 (the amino acid sequences of SEQ ID NOs:14-18). Thus, Hartman does not teach each and every element of claim 2 (new claim 54).

Included herewith is an amendment to the claims such that the subject matter of claims 9-11 has been canceled, making the rejection moot with regard to these claims.

Because Hartman does not teach each and every element of claims 1-3 (new claims 53, 54 and 71), and in view of the cancellation of the subject matter of claims 9-11, Applicants respectfully request reconsideration and withdrawal of this rejection.

C. At paragraph 12 of the Office Action, claims 1-6 and 9-11 are rejected under 35 U.S.C. §102(e) as being anticipated by Kufe et al. (U.S. Patent Publication No. 2005/0053606, filed Sept. 11, 2001).

Briefly, the Examiner states that Kufe teaches antibodies that bind to the non-shed extracellular domain of Muc1, specifically a portion of SEQ ID NO:1, and to humanized versions of the antibodies.

Included herewith is an amendment to the claims such that claim 1 has been replaced by new claim 53 which recites antibodies that bind to specific portions of Muc1 (the amino acid sequences of SEQ ID NOs:8, 9, 10 and 12).

Kufe does not teach antibodies that bind to any of the portions of Muc1 recited in new claim 53 (SEQ ID NOs:8, 9, 10 and 12). As shown in Appendix B, Kufe teaches a 45 amino acid portion of Muc1 (MUC1/ECD). This peptide sequence is encompassed within the non-shed extracellular domain of Muc1 identified by Applicants (SEQ ID NO:1), shown as the dashed line from 1 to 45 above Applicants' sequence ("Payne SEQ ID NO:1"). Kufe teaches two antibodies that bind to specific portions of Muc1, shown as bold in the "Payne SEQ ID NO:1" sequence in Appendix B.

The three portions of Muc1 recited in new claim 53 (SEQ ID NOs:8, 9, 12) that are encompassed within the sequence taught by Kufe are shown in Appendix B as a single underline, a double underline and a dashed underline.

A comparison of the epitopes recognized by the antibodies of Kufe, with those recognized by the antibodies of new claim 53 (bold sequences compared to the underscored sequences), reveals that none of the Kufe epitopes corresponds to the epitopes recited in new

claim 53. As such, the skilled artisan would not expect the antibodies of Kufe to bind the epitopes recited in new claim 53. Accordingly, Kufe does not teach each and every element of new claim 53.

Kufe also does not teach a hybridoma that produces an antibody of claim 1 (new claim 53), and thus does not teach each and every element of claim 3 (new claim 71). Kufe also does not teach the types of antibodies recited in claim 4 (new claim 55).

Furthermore, Kufe does not teach antibodies that bind to Muc16. Claim 2 has been replaced by new claim 54 which recites antibodies that bind to specific portions of Muc16 (the amino acid sequences of SEQ ID NOs:14-18). Thus, Kufe does not teach each and every element of claim 2 (new claim 54).

Included herewith is an amendment to the claims such that the subject matter of claims 5, 6 and 9-11 has been canceled, making the rejection moot with regard to these claims.

Because Kufe does not teach each and every element of claims 1-4 (new claims 53, 54, 71 and 55), and because the subject matter of claims 5, 6 and 9-11 has been canceled, Applicants respectfully request reconsideration and withdrawal of this rejection.

IV. Rejection Under 35 U.S.C. §103

A. At paragraph 14 of the Office Action, claims 1-8 and 15-19 are rejected under 35 U.S.C. §103(a) as being unpatentable over Radosevich et al. in view of Mack et al. (U.S. Patent Publication No. 2004/0146862, filed April 9, 2001), in view of Chari et al. (a) (USP 6,333,410, issued Dec. 25, 2001), in view of Chari et al. (b) (USP 6,340,701, issued Jan. 22, 2000) and in view of Chari et al. (c) (USP 5,846,545, issued Dec. 8, 1998), and further in view of Ni et al. (U.S. Patent Publication No. 2003/0170237, filed April 30, 1998).

Briefly, the Examiner states that Radosevich teaches monoclonal antibodies to an antigen that is not found in serum, and thus Radosevich anticipates claims to an antibody that specifically binds to an epitope of a non-shed extracellular portion of a shed antigen as recited in claim 1 (see paragraph 10 of the office action). The Examiner admits that Radosevich does not specifically teach the antibody variants recited in claim 4, the use of a carrier as recited in claim 5, a fusion

protein as recited in claims 6 and 7, or a cytotoxic conjugate as recited in claims 15-19. The Examiner states that the additional art cited in this rejection provides the missing elements recited in claims 4-7 and 15-19, and that it would have been *prima facie* obvious to combine the cited art to arrive at the invention as recited in these claims.

As discussed above, included herewith is an amendment to the claims such that claim 1 has been replaced by new claim 53 which recites antibodies that bind to specific portions of Muc1 (the amino acid sequences of SEQ ID NOs:8, 9, 10 and 12), and claim 2 has been replaced by new claim 54 which recites antibodies that bind to specific portions of Muc16 (the amino acid sequences of SEQ ID NOs:14-18). Radosevich does not teach antibodies that bind to any portion of Muc1 or Muc16, let alone the portions of Muc1 set forth in SEQ ID NOs:8, 9, 10 and 12, or the portions of Muc16 set forth in SEQ ID NOs:14-18.

Nor does Radosevich teach hybridomas that produce antibodies of claims 1 or 2 (new claims 53 and 54), as recited in claim 3 (new claims 71 and 72). Radosevich also does not teach the specific types of antibodies recited in claim 4 (new claim 55), or the conjugates or compositions of claims 15-19 (new claims 56-60). The subject matter of claims 5-8 has been canceled.

None of the additional art cited by the Examiner teaches antibodies that bind to Muc1 or Muc16, or antibodies that bind to the specific portions of Muc1 or Muc16 recited in new claims 53 and 54.

Accordingly, Radosevich does not teach each and every element of the claims as amended herein, alone or in combination with the additional art cited by the Examiner. The Examiner has therefore not made a *prima facie* showing of obviousness and Applicants respectfully request reconsideration and withdrawal of this rejection.

B. At paragraph 15 of the Office Action, claims 1-11 and 15-19 are rejected under 35 U.S.C. §103(a) as being unpatentable over Hartman et al., as evidenced by Zrihan-Licht et al. and Parry et al., and in view of Mack et al., in view of Chari et al. (a), in view of Chari et al. (b) and in view of Chari et al. (c), and further in view of Ni et al.

The Examiner states that while Hartman teaches antibodies to a non-shed extracellular portion of a shed antigen, Hartman does not specifically teach the antibody variants recited in claim 4, a fusion protein as recited in claims 6 and 7, or a cytotoxic conjugate as recited in claims 15-19. The Examiner states that the additional art cited in this rejection teaches the missing elements recited in claims 4, 6-7 and 15-19, and that it would have been *prima facie* obvious to combine the cited art to arrive at the instant invention.

As discussed above, Hartman does not teach the antibodies of claims 1 and 2 (new claims 53 and 54). Hartman also does not teach a hybridoma that produces an antibody of claim 1 or 2, as recited in claim 3 (new claims 71 and 72), or the specific antibody types of claim 4 (new claim 55). The subject matter of claims 5-11 has been canceled. Hartman also does not teach conjugates or compositions comprising the antibodies of claim 1 or 2 (new claims 53 and 54), as recited in claims 15-19 (new claims 56-60).

Nor does any of the additional art cited by the Examiner teach the antibodies of claim 1 or 2 (new claims 53 and 54), the hybridomas of claim 3 (new claims 71 and 72), the antibody types of claim 4 (new claim 55), or the conjugates and compositions of claims 15-19 (new claims 56-60).

Accordingly, Hartman does not teach each and every element of the cited claims, alone or in combination with the additional art cited by the Examiner. The Examiner has therefore not made a *prima facie* showing of obviousness and Applicants respectfully request reconsideration and withdrawal of this rejection.

C. At paragraph 16 of the Office Action, claims 1-8 and 12-19 are rejected under 35 U.S.C. §103(a) as being unpatentable over Mitcham et al. (WO 02/06317, filed July 17, 2001) as evidenced by the instant application (page 1, paragraph 3) and as evidenced by Albone et al. (U.S. Patent Publication No. 2005/0064518, filed Oct. 16, 2002) in view of Weiner et al. (USP 6,512,096, filed June 25, 1998), as evidenced by Thorpe et al. (USP 5,776,427, issued July 7, 1998), and in view of Hoogenbooom et al. (U.S. Patent Publication No. 2003/0235868, filed April 22, 2002), and in view of Mack et al., in view of Chari et al. (a), in view of Chari et al. (b) and in view of Chari et al. (c), and further in view of Ni et al.

The Examiner states that the claims encompass antibodies that bind an epitope located within the carboxy-terminal 110 amino acids of the extracellular domain of Muc16, specifically SEQ ID NO:2, or one of the portions of SEQ ID NO:2 set forth in SEQ ID NOs:14-18.

The Examiner states that Mitcham teaches the extracellular portion of O772P, which is the same as CA125 (Muc16), that is retained on the plasma membrane of a cell after cleavage, and that Mitcham suggests O772P is an attractive target for therapeutic antibodies. The Examiner further states that Mitcham teaches the predicted extracellular domain of O772P, and that cleavage likely occurs at position 10 of SEQ ID NO:489.

The Examiner states that it would have been obvious to produce antibodies that bind to the non-shed extracellular portion of O772P based on the teachings of Mitcham and Weiner. The Examiner explains that the skilled artisan would have been motivated to make anti-O772P antibodies because Mitcham teaches that the extracellular portion of O772P retained on the cell is "attractive target for directing specific immunotherapies, e.g., therapeutic antibodies, against this protein." The Examiner further states that the skilled artisan would have had a reasonable expectation of success in producing anti-O772P antibodies that bind to an epitope of this domain because Weiner teaches the production of highly specific antibodies.

As discussed above, included herewith is an amendment to the claims such that claim 2 has been replaced by new claim 54 which recites antibodies that bind to specific portions of Muc16 (the peptides of SEQ ID NOs:14-18).

Neither Mitcham or any of the additional art cited by the Examiner teaches antibodies having the particular binding specificity recited in new claim 54. Nor is there any direction in the art cited by the Examine that would lead one of ordinary skill in the art to produce antibodies against the five portions of Muc16 as recited in new claim 54.

Mitcham also does not teach antibodies that bind to the specific portions of Muc1 recited in claim 1 (new claim 53), or hybridomas that produces an antibody of claim 1 or 2 (new claims 53 and 54), as recited in claim 3 (new claims 71 and 72), or the specific antibody types of claim 4 (new claim 55). The subject matter of claims 5-8 and 12-14 has been canceled. Mitcham also

does not teach conjugates or compositions comprising the antibodies of claim 1 or 2 (new claims 53 and 54), as recited in claims 15-19 (new claims 56-60).

Nor does any of the additional art cited by the Examiner teach the antibodies of claim 1 or 2 (new claims 53 and 54), the hybridomas of claim 3 (new claims 71 and 72), the antibody types of claim 4 (new claim 55), or the conjugates and compositions of claims 15-19 (new claims 56-60).

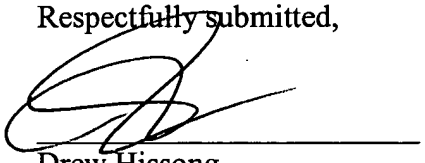
Accordingly, Mitcham does not teach each and every element of the cited claims, alone or in combination with the additional art cited by the Examiner. The Examiner has therefore not made a *prima facie* showing of obviousness and Applicants respectfully request reconsideration and withdrawal of this rejection.

V. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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WASHINGTON OFFICE
23373
CUSTOMER NUMBER

Date: June 20, 2006

APPENDIX A

MucI/Y

```
                                                  1
       Signal peptide                             ↓
MTPGTQSPFF LLLLLTVLTV VTGSGHASST PGGEKETSAT

                          30---------------6E6/2--------------------------
                          ↓
QRSSVPSSTE KNAFNSSLED PSTDYYQELQ RDISEMFLQI
                                                                  ↑
                                                                  1-----

---------------------67 68-------7D10/4, 9G2/6, 6C4/5------87 88------------
                      ↓ ↓                                     ↓ ↓
YKQGGFLGLS NIKFRPGSVV VQLTLAFREG TINVHDVETQ
                              ↑         ↑
------------------------------21        26---------------------------------

----6D3/12-------------108                 118---------10D2/36------131
                        ↓                   ↓                       ↓
FNQYKTEAAS RYNLTISDVS VSDVPFPFSA QSGAGVPGWG
  ↑ ↑                                   ↑ ↑
-46 47-----------------------------------67 68-----------------------------

IALLVLVCVL VALAIVYLIA LAVCQCRRKN YGQLDIFPAR
  ↑
--86

DTYHPMSEYP TYHTHGRYVP PSSTDRSPYE KVSAGNGGSS

LSYTNPAVAA TSANL
```

Payne et al. portions of Muc1

1-21 - SEQ ID NO:10

26-46 - SEQ ID NO:8

47-67 - SEQ ID NO:9

68-86 - SEQ ID NO:12

APPENDIX B

Kufe SEQ ID NO:1 (MUC1/ECD)

TINVHDVETQFNQYKTEAASRYNLTISDVSVSDVPFPFSAQSGAG

Payne SEQ ID NO:1

1----------

FLQIYKQGGFLGLSNIKFRPGSVVVQLTLAFREGTINV**HDVETQFNQ**

----------45

YKTEAASRYNLTI**SDVSVSDVPFPFSAQS**GAGVPGWGIA

QLTLAFREGTINVHDVETQFN (Payne SEQ ID NO:8)

QYKTEAASRYNLTISDVSVSD (Payne SEQ ID NO:9)

VPFPFSAQSGAGVPGWGIA (Payne SEQ ID NO:12)

HDVETQFNQYKTEAAS (Kufe SEQ ID NO:4)

SDVSVSDVPFPFSAQS (Kufe SEQ ID NO:7)